

CLAIMS

1. A method of treating a mammal having an immunological renal disorder,
comprising administering to the mammal an effective amount of a composition
5 comprising an inhibitor of the LT pathway, thereby treating the mammal.
2. The method of claim 1, wherein the disorder is selected from the group
consisting of systemic lupus erythematosus, Sjogren's syndrome, rheumatoid
arthritis, insulin dependent diabetes mellitus, chronic hepatitis,
10 Henoch-Schonlein purpura, and IgA nephropathy.
3. The method of claim 1, wherein the disorder IgA nephropathy.
4. The method of claim 1, wherein the mammal is human.
- 15 5. The method of claim 1, wherein the inhibitor is a LTBR antibody or a LT
antibody.
6. The method of claim 1, wherein the inhibitor comprises a polypeptide.
- 20 7. The method of claim 6, wherein the polypeptide comprises the amino acid
sequence of SEQ ID NO:1, or a portion thereof.
8. The method of claim 6, wherein the polypeptide comprises:
25 (a) the amino acid sequence of SEQ ID NO:1; or
(b) an amino acid sequence encoded by a nucleic acid that is at least 100,
200, 300, 400, or 500 nucleotides long and hybridizes to the nucleic acid
encoding (a) under defined conditions; and wherein the polypeptide inhibits
immunoglobulin secretion by B cells.
- 30 9. The method of claim 8, wherein the defined conditions comprise pretreating for 8
hours at 65°C in a solution comprising 6 x SSC, 50 mM Tris-HCl (pH 7.5), 1
mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.02% BSA, and 500 µg/ml denatured

salmon sperm DNA; hybridizing for 48 hours at 65°C; and washing for 1 hour at 37°C in a solution comprising 2 x SSC, 0.01% PVP, 0.01% Ficoll, and 0.01% BSA and for 45 minutes at 50°C in a solution comprising 0.1 x SSC.

- 5 10. The method of claim 8, wherein the polypeptide further comprises a Fc fragment of IgG1 or a Fc fragment of IgG4.
11. The method of claim 1, wherein the inhibitor comprises a soluble LTBR fused to one or more heterologous protein domains.
- 10 12. The method of claims 11, wherein the soluble LTBR comprises a ligand binding domain that can selectively bind to a lymphotoxin (LT) ligand comprising at least one LT beta subunit.
- 15 13. The method of claims 11, wherein the soluble LTBR comprises an extracellular domain of LT-beta-R.
14. The method of claims 11, wherein the soluble LTBR is human LT-beta-R.
- 20 15. The method of claim 11, wherein the heterologous protein domain comprises a human immunoglobulin Fc domain.
16. A method of treating a subject with glomerulonephritis, comprising administering to the subject an effective amount of a composition comprising an inhibitor of the LT pathway, thereby treating the glomerulonephritis.
- 25 17. The method of claim 16, wherein the glomerulonephritis is associated with a disorder is selected from the group consisting of systemic lupus erythematosus, Sjogren's syndrome, rheumatoid arthritis, insulin dependent diabetes mellitus, chronic hepatitis, Henoch-Schonlein purpura, and IgA nephropathy.
- 30 18. The method of claims 16 or 17, wherein the inhibitor comprises a soluble LTBR fused to one or more heterologous protein domains.

19. The method of claims 16 or 17, wherein the inhibitor comprises a soluble LTBR comprising a functional sequence of amino acids selected from the amino acids of SEQ ID NO: 1.
- 5 20. The method of claims 16 or 17, wherein the soluble LTBR comprises a ligand binding domain that can selectively bind to a surface lymphotoxin (LT) ligand comprising at least one LT beta subunit.
21. The method of claims 16 or 17, wherein the soluble LTBR comprises an
10 extracellular domain of LT-beta-R.
22. The method of claims 16 or 17, wherein the soluble LTBR is human LT-beta-R.
- 23 The method of claim 18, wherein the heterologous protein domain comprises a
15 human immunoglobulin Fc domain.
24. A method of evaluating the efficacy of a compound for treatment of IgA nephropathy, comprising: administering the compound to a BAFF-transgenic animal; and determining the test level of IgA deposits in a kidney of the animal
20 after administration; and comparing the level with a threshold level, wherein a test level lower than the threshold level indicates that the compound is efficacious.
25. The method of claim 24, wherein the animal is a rodent.
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